[CANCER RESEARCH 55, 4899–4905, November 1, 1995]

Alcohol and Pancreatic Cancer in Blacks and Whites in the United States[1]

Debra T. Silverman,[2] Linda M. Brown, Robert N. Hoover, Mark Schiffman, Keith D. Lillemoe, Janet B. Schoenberg, G. Marie Swanson, Richard B. Hayes, Raymond S. Greenberg, Jacques Benichou, Ann G. Schwartz, Jonathan M. Liff, and Linda M. Pottern

Epidemiology and Biostatistics Program, National Cancer Institute, Bethesda, Maryland 20892 [D. T. S., L. M. B., R. N. H., M. S., R. B. H., J. B., L. M. P.]; Department of Surgery, the Johns Hopkins University School of Medicine, Baltimore, Maryland 21205 [K. D. L.]; Special Epidemiology Program, New Jersey State Department of Health, Trenton, New Jersey 08625 [J. B. S.]; College of Human Medicine, Michigan State University, East Lansing, Michigan 48824 [G. M. S.]; Medical University of South Carolina, Charleston, South Carolina 29425-1020 [R. S. G.]; Division of Epidemiology, Emory University School of Public Health, Atlanta, Georgia 30329 [J. M. L.]; and Department of Clinical Epidemiology and Family Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15261 [A. G. S.]

ABSTRACT

A population-based, case-control study of pancreatic cancer based on direct interviews with 307 white and 179 black incident cases and 1164 white and 945 black population controls was conducted in three areas of the United States to determine the role alcohol drinking plays as a risk factor for pancreatic cancer and to estimate the extent to which it may explain the higher incidence of pancreatic cancer in blacks compared to whites. Our findings indicate that alcohol drinking at the levels typically consumed by the general population of the United States is probably not a risk factor for pancreatic cancer. Our data suggest, however, that heavy alcohol drinking may be related to pancreatic cancer risk. Among men, blacks and whites who drank at least 57 drinks/week had odds ratios (ORs) of 2.2 [95% confidence interval (CI) = 0.9–5.6] and 1.4 (95% CI = 0.6–3.2), respectively. Among women, blacks who drank 8 to <21 drinks/week had an OR of 1.8 (95% CI = 0.8–4.0), and those who drank at least 21 drinks/week had an OR of 2.5 (95% CI = 1.02–5.9), but whites with the same levels of alcohol intake experienced no increased risk. Compared to whites, blacks had significantly higher ORs associated with heavy alcohol drinking (≥57 drinks/week) in men ($P = 0.04$) and with moderate-to-heavy drinking (≥8 drinks/week) in women ($P = 0.03$). Additional research is needed to determine whether heavy alcohol drinking is causally related to pancreatic cancer and whether the risk of alcohol-related pancreatic cancer is greater in blacks than in whites.

INTRODUCTION

For several decades, black Americans consistently have experienced more than a 50% higher risk of pancreatic cancer than whites (1). During the time period 1986–1990, United States average annual age-adjusted incidence rates of pancreatic cancer were 13.8/100,000 for blacks and 8.8/100,000 for whites (2). Because the etiology of pancreatic cancer is not well understood, the reasons for this excess among blacks are unclear. Alcohol drinking has been associated with increased risk of pancreatic cancer in at least 15 epidemiological studies (3–17), but this association has not been observed in at least 21 other studies (18–25). Our purpose is to further investigate the role alcohol plays as a risk factor for pancreatic cancer and to estimate the extent to which it may explain the black/white difference in incidence rates. This is the first study of pancreatic cancer to include a sufficient number of blacks to address this issue.

MATERIALS AND METHODS

This population-based, case-control study was initiated simultaneously with case-control studies of three other malignancies that also occur excessively in blacks (*i.e.*, esophagus, prostate, multiple myeloma). One general population control group provided controls for all four types of cancer.

Cases were identified through population-based cancer registries in Detroit (Macomb, Oakland, and Wayne Counties), New Jersey (10 counties), and Atlanta (DeKalb and Fulton Counties). Our case series consisted of all incident cases of carcinoma of the pancreas (International Classification of Diseases, 0 = 157) first diagnosed from August 1986 to April 1989 among residents of these study areas, ages 30–79 years. To ensure the population-based nature of our case series and to identify as completely as possible all cases of pancreatic cancer, we included cases regardless of whether they had tissue confirmation. Because about 15% of our cases lacked tissue confirmation, in-depth medical chart reviews were conducted independently on all cases to determine accuracy of diagnosis. Overall, only 4.9% of white and 6.6% of black cases were found to be "unlikely" to have had pancreatic cancer and were excluded from all analyses.

Of the 713 white and 440 black cases eligible for study, interviews were obtained for 331 whites (46%) and 195 blacks (44%). Because of the poor prognosis of this tumor, the primary reason for nonresponse was death. Two hundred seventy-one white (38%) and 200 (45%) black cases had died before an interview could be conducted, despite the emphasis placed on ascertaining and interviewing cases within 6 weeks of diagnosis. (The median time from diagnosis to interview was 51 days for white cases and 47 days for black cases.) Other reasons for nonresponse were physician or patient refusal [34 white (5%) and 17 black (4%) cases], severe illness [64 white (9%) and 25 black (6%) cases], and language or other problems [13 white (2%) and 3 black (1%) cases].

Our control series was drawn from the general population of the study areas, frequency matching controls to the expected age-race-sex distribution of cases of all four types of cancer combined in each study area. The age matching was done in 5-year age groups. Controls 30–64 years old were chosen by a method of random-digit dialing (26). Of the 17,746 households telephoned, 86% provided a household census that served as the basis for a sampling frame for control selection. Of the 895 white and 673 black controls selected from these households, 701 white (78%) and 526 black (78%) controls were interviewed. One hundred forty-nine white (17%) and 109 black (16%) controls refused to participate, 12 white (1%) and 11 black (2%) controls were too ill, 3 white (.3%) and 2 black (.3%) controls had died, and 30 white (3%) and 25 black (4%) controls did not speak English or were unable to participate for other reasons.

Controls 65–79 years old consisted of a stratified random sample drawn from lists from the Health Care Financing Administration of the population age 65 years and older in each study area. Of the 656 white and 576 black older controls selected, interviews were obtained for a total of 479 whites (73%) and 447 blacks (78%). One hundred nineteen white (18%) and 58 black (10%) older controls refused to participate, 29 whites (4%) and 34 blacks (6%) were too ill, 7 whites (1%) and 15 blacks (3%) had died, and 22 whites (3%) and 22 blacks (4%) did not speak English or were unable to participate for other reasons.

Interviews were usually conducted in the home of the subject by a trained interviewer. Before the interview, written informed consent to participate in the study was obtained from each subject. The questionnaire was designed to obtain detailed information on alcohol consumption, smoking history, coffee and tea consumption, dietary factors, medical conditions, usual occupation, family history of cancer, and socioeconomic status.

Alcohol drinkers were defined as subjects who reported ever drinking at least 1 drink of hard liquor, beer, or wine per month for at least 6 months. The

Received 11/28/94; accepted 8/25/95.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

[1] This research was performed under National Cancer Institute contracts N01-CP-51090, N01-CP-51089, N01-CP-51092, N01-CN-05225, N01-CN-31022, and N01-CN-05227.

[2] To whom requests for reprints should be addressed, at Epidemiology and Biostatistics Program, National Cancer Institute, NIH, Executive Plaza North, Room 418, Bethesda, MD 20892.

Table 1 *Numbers of cases and controls and ORs for pancreatic cancer according to total alcohol consumption by race and sex*

Total alcohol consumption	White				Black			
	No. of cases	No. of controls	OR[a]	95% CI	No. of cases	No. of controls	OR[a]	95% CI
Men[b]								
Never drank	38	152	1.0		14	137	1.0	
Ever drank	128	589	0.9	0.6–1.4	66	462	1.0	0.5–1.9
No. of drinks/wk[c,d]								
Never drank	38	152	1.0		14	137	1.0	
1–<8	40	216	0.8	0.5–1.4	11	129	0.6	0.2–1.6
8–<22	39	204	0.8	0.4–1.3	24	164	1.2	0.5–2.6
22–<57	32	132	1.0	0.6–1.9	13	122	0.6	0.2–1.6
≥57	15	37	1.4	0.6–3.2	17	46	2.2	0.9–5.6
							($P = 0.04$)[e]	
Women[f]								
Never drank	85	222	1.0		50	226	1.0	
Ever drank	56	201	0.6	0.4–0.97	44	120	1.5	0.9–2.7
No. of drinks/wk[c,d]								
Never drank	85	222	1.0		50	226	1.0	
1–<8	34	138	0.7	0.4–1.1	14	66	1.1	0.5–2.2
8–<21	15	52	0.4	0.2–0.9	17	34	1.8	0.8–4.0
≥21	7	11	0.9	0.3–3.0	13	20	2.5	1.02–5.9
							($P = 0.03$)[e]	

[a] ORs adjusted for age, area, cigarette smoking, gallbladder disease, and diabetes.
[b] ORs also adjusted for income.
[c] One drink = 1.5 ounces of hard liquor, 12 ounces of beer, or 4 ounces of wine.
[d] Three cases and 1 control with missing information on amount of alcohol consumed were excluded from estimation of risk by amount consumed.
[e] P value for test of linear trend.
[f] ORs also adjusted for obesity.

usual number of drinks per week for each type of alcoholic beverage was derived from the questionnaire data on weekday and weekend usual adult consumption of each type of alcoholic beverage. The number of glasses, bottles, and cans of each type of alcohol reported by the subject was converted into number of drinks based on the following equivalencies: 1 drink = 1.5 ounces of hard liquor = 4 ounces of wine = 12 ounces of beer.

The association between alcohol consumption and pancreatic cancer risk was quantified by the "relative risk" as estimated by the OR.[3] ORs and two-sided 95% CIs were estimated by unconditional logistic regression analyses (27, 28). Race- and sex-specific models included terms for alcohol drinking, age, and study area, as well as terms for potential confounders [*i.e.*, cigarette smoking as measured by usual amount smoked per day, gallbladder disease, diabetes mellitus, obesity (women only) as measured by body mass index (29), and income (men only)]. Of these confounders, adjustment for cigarette smoking had the greatest impact on point estimates. Additional adjustments for pancreatitis and several dietary risk factors (*i.e.*, complex and simple carbohydrate intake and vegetable consumption) had little or no impact on point estimates (*i.e.*, adjustment changed the point estimate by less than 10%) and were not included in final models. To test for trend, the exposure variable was treated as continuous in the model by entering the median value for each level of the categorical variable among the controls. One-sided significance tests of the interaction between race and alcohol drinking were used because the *a priori* alternative hypothesis was that blacks have higher alcohol-related ORs than do whites. PARs and the two-sided 95% CIs were computed by the methods of Bruzzi *et al.* (30) and Benichou and Gail (31), respectively, and were adjusted for age, geographic area, smoking, income (men only), gallbladder disease, diabetes mellitus, and obesity (women only).

Interviewed subjects were excluded from analysis for the following reasons: 16 cases were unlikely to have had pancreatic cancer, 10 cases had islet cell carcinomas, 6 cases had no medical record available for review, 1 case and 7 controls had interviews that were judged unsatisfactory by the interviewer, and 7 cases and 37 controls had missing data. The alcohol analysis was based on first-person interviews with 486 (307 white and 179 black) "likely" cases with a diagnosis of carcinoma of the exocrine pancreas and 2109 (1164 white and 945 black) population controls.

[3] The abbreviations used are: OR, odds ratio; CI, confidence interval; PAR, population-attributable risk; HIS, National Health Interview Survey.

RESULTS

Our case series experienced the poor survival and low response rate that typically accompany highly fatal diseases such as pancreatic cancer. Because many patients had died before an interview was possible, we were concerned about the representativeness of the case series with regard to the exposures under study. To address this concern, we conducted interviews with next of kin of a sample of cases who died (*i.e.*, 210 white and 115 black deceased cases) to determine the comparability of those who died and those who lived long enough to be interviewed. The next-of-kin interview was restricted to broad questions that next-of-kin respondents have been shown to answer reliably (32). The overall percentage of cases who ever drank alcohol regularly as reported by next-of-kin respondents was similar to that reported by directly interviewed cases (white men, 74% and 77%; black men, 88% and 83%; white women, 48% and 41%; black women, 54% and 46%, respectively). Next-of-kin data also tended to be similar to data from interviewed cases for each type of alcoholic beverage, suggesting that alcohol consumption as reported by interviewed cases was probably representative of the alcohol-drinking patterns in the total case series.

Total Alcohol Consumption. Among men, blacks and whites had similar percentages of population controls who ever drank any type of alcohol (77 *versus* 79%). Among women, however, a significantly ($P < 0.01$) lower percentage of black than white controls ever drank alcohol (35 *versus* 48%). In contrast, black controls had higher percentages of heavy drinkers than did white controls for both men and women [men who drank ≥ 57 drinks per week; 8 *versus* 5% ($0.01 < P < 0.05$); women who drank ≥ 21 drinks per week, 6 *versus* 3% ($0.01 < P < 0.05$)].

Table 1 shows risk of pancreatic cancer associated with total alcohol consumption. No association with ever drinking alcohol was apparent among men of either race. Black women experienced a nonsignificant 50% increased risk of pancreatic cancer associate

with ever having consumed alcohol, and white women experienced a marginally significant 40% reduced risk.

Significant trends in risk with increasing total alcohol intake were apparent for blacks but not whites (black men, $P = 0.04$; black women, $P = 0.03$). Although the trend was significant among black men, no evidence of a monotonic increase in risk was seen with increasing intake. Rather, risk was restricted to heavy drinkers; those who drank at least 57 drinks/week had an OR of 2.2 (95% CI = 0.9–5.6) compared to 1.4 for white men (95% CI = 0.6–3.2). Among black women, the trend in risk with increasing total alcohol consumption was monotonic as well as significant. Black women who drank 8 to <21 drinks/week had an OR of 1.8 (95% CI = 0.8–4.0), and those who drank at least 21 drinks/week had an OR of 2.5 (95% CI = 1.02–5.9) compared to ORs of 0.4 and 0.9, respectively, for white women. The interactions between race and both heavy alcohol intake (≥57 drinks/week) in men and moderate-to-heavy intake (≥8 drinks/week) in women were statistically significant (men, $P = 0.04$; women, $P = 0.03$).

Hard Liquor Consumption. Pancreatic cancer risk according to hard liquor consumption is shown in Table 2. No significant trends in risk with increasing hard liquor intake were observed. Heavy hard liquor drinking (>35 drinks/week), however, was associated with increased risk in black men (OR = 2.4; 95% CI = 0.9–6.3) but not in white men. Black women experienced an overall excess risk associated with hard liquor consumption (OR = 1.8; 95% CI = 0.9–3.3), whereas white women experienced no overall elevation in risk.

We examined several additional variables related to hard liquor consumption: type of liquor, amount of dilution, and binge drinking. None of these variables appeared related to risk either as a risk factor or an effect modifier.

Beer Consumption. Table 3 gives the ORs for pancreatic cancer associated with beer drinking. White men had a significant positive trend in risk with increasing beer intake ($P = 0.02$). The trend was inconsistent, however. The increased risk was limited to white men who drank more than 28 beers/week (OR = 2.1; 95% CI = 1.03–4.2). In contrast, black men experienced no increased risk associated with beer drinking. Among women, there was little or no elevation in overall risk for either blacks or whites. Black women who drank more than 7 beers/week did have a nonsignificant 60% elevation in risk, but white women had no increased risk associated with beer drinking.

Wine Consumption. ORs for pancreatic cancer according to wine consumption are given in Table 4. No significant trends in risk with increasing wine intake were apparent. Moderate-to-heavy wine intake in black men was associated with a nonsignificant 60% elevation in risk, whereas white men experienced no elevated risk. Among women, little or no overall increased risk was apparent for either black or white drinkers of wine. White women who drank at least 7 glasses/week did experience a nonsignificant 40% elevation in risk, whereas moderate-to-heavy black female drinkers experienced no risk elevation.

Alcohol Drinking in Nonsmokers. Despite the inclusion of terms for cigarette smoking in all models, we were concerned about residual confounding by smoking, a risk factor for pancreatic cancer (33) and a strong correlate of alcohol drinking. To address this concern, we examined alcohol effects among lifelong nonsmokers when numbers permitted. For white nonsmokers, patterns of risk were similar to those observed for the total group of whites. For black nonsmokers, however, some alcohol effects were stronger than those observed for the total group of blacks.

Black male nonsmokers experienced an increased risk associated with heavy beer drinking, which was not apparent in the total group of black men. Those who drank more than 14 beers/week had an OR of 2.2 (95% CI = 0.4–12.2). The effect of hard liquor was also greater in nonsmokers. Black male nonsmokers who drank more than 14 drinks/week had an OR of 5.6 (95% CI = 1.1–28.3). There were too few black male wine drinkers to estimate risk among nonsmokers.

Black female nonsmokers also experienced stronger effects for both total alcohol drinking and beer drinking than those observed for the total group of black women. Black female nonsmokers had ORs of 2.6 (95% CI = 1.1–6.1) for ever drinking alcohol and 4.8 (95% CI = 1.5–15.1) for drinking at least 8 drinks/week. For beer drinking, ORs were 3.0 (95% CI = 0.9–10.0) for ever drinkers and 6.0 (95% CI = 1.0–36.4) for drinkers of more than 14 beers/week. The effects of hard liquor were similar to those observed for total black women. There were too few black female wine drinkers to estimate risk in nonsmokers.

Table 2 *Numbers of cases and controls and ORs for pancreatic cancer according to hard liquor consumption by race and sex*

Hard liquor consumption	White				Black			
	No. of cases	No. of controls	OR[a]	95% CI	No. of cases	No. of controls	OR[a]	95% CI
Men[b]								
Never drank liquor	83	337	1.0		23	220	1.0	
Ever drank liquor	83	404	0.8	0.5–1.2	57	379	1.2	0.6–2.3
No. of drinks/wk[c]								
Never drank liquor	83	337	1.0		23	220	1.0	
1–≤7	48	251	0.9	0.5–1.4	13	136	0.9	0.4–2.0
8–≤14	11	76	0.7	0.3–1.4	11	92	1.2	0.5–3.0
15–≤35	17	56	0.9	0.5–1.9	19	103	1.2	0.5–2.7
>35	4	15	0.5	0.1–2.0	12	37	2.4	0.9–6.3
							($P = 0.06$)[d]	
Women[e]								
Never drank liquor	104	294	1.0		58	271	1.0	
Ever of drank liquor	37	129	0.7	0.4–1.2	36	75	1.8	0.9–3.3
No. of drinks/wk[c]								
Never drank liquor	104	294	1.0		58	271	1.0	
1–≤7	26	106	0.6	0.3–1.2	17	46	1.6	0.8–3.4
8–≤14	7	15	0.9	0.3–2.8	13	12	2.8	1.0–8.1
>14	4	8	0.8	0.2–3.0	6	16	1.2	0.4–3.9

[a] ORs adjusted for age, area, cigarette smoking, gallbladder disease, diabetes, beer consumption, and wine consumption.
[b] ORs also adjusted for income.
[c] Five cases and 18 controls with missing information on amount of hard liquor consumed were excluded from estimation of risk by amount consumed.
[d] P value for test of linear trend.
[e] ORs also adjusted for obesity.

Table 3 *Numbers of cases and controls and ORs for pancreatic cancer according to beer consumption by race and sex*

Beer consumption	White				Black			
	No. of cases	No. of controls	OR[a]	95% CI	No. of cases	No. of controls	OR[a]	95% CI
Men[b]								
Never drank beer	65	270	1.0		33	246	1.0	
Ever drank beer	101	471	0.9	0.6–1.4	47	353	0.8	0.4–1.4
No. of beers/wk[c]								
Never drank beer	65	270	1.0		33	246	1.0	
1–≤7	47	249	0.8	0.5–1.3	22	190	0.9	0.5–1.8
8–≤14	10	95	0.5	0.2–1.0	7	78	0.4	0.1–1.2
15–≤28	17	71	1.1	0.6–2.3	10	52	1.0	0.4–2.4
>28	22	50	2.1	1.03–4.2	6	23	0.9	0.3–2.9
			(P = 0.02)[d]					
Women[e]								
Never drank beer	118	356	1.0		63	267	1.0	
Ever drank beer	23	67	0.9	0.5–1.7	31	79	1.2	0.7–2.4
No. of beers/wk[c]								
Never drank beer	118	356	1.0		63	267	1.0	
1–≤7	16	52	1.0	0.5–2.1	17	55	1.1	0.5–2.3
>7	7	15	0.7	0.2–2.0	14	23	1.6	0.6–3.9

[a] ORs adjusted for age, area, cigarette smoking, gallbladder disease, diabetes, hard liquor consumption, and wine consumption.
[b] ORs also adjusted for income.
[c] Seven cases and 17 controls with missing information on amount of beer consumed were excluded from estimation of risk by amount consumed.
[d] P value for test of linear trend.
[e] ORs also adjusted for obesity.

Attributable Risks. If heavy alcohol drinking is, in fact, causally related to pancreatic cancer risk, the proportion of the black excess that may be attributable to alcohol consumption is estimable. Our intent is to use the PAR as an analytic tool to quantify the proportion of the black excess that may be attributable to heavy alcohol drinking if heavy drinking is confirmed as a risk factor for pancreatic cancer. It would not be appropriate to use the PARs estimated from these data to make public health recommendations.

For meaningful PAR estimation, it is important to define exposure to capture the observed increase in risk. Because the levels of alcohol consumption associated with increased risk were higher in men than women (*i.e.*, men, ≥57 drinks/week; women, ≥8 drinks/week), we used different definitions of exposure to alcohol for each sex.

Table 5 shows PARs for alcohol drinking by race and sex. Among men, 11% of pancreatic cancer in blacks may be attributable to heavy alcohol consumption compared to 2% in whites. The PAR was higher in blacks for two reasons: (*a*) the OR was higher in blacks than whites (2.2 *versus* 1.4); and (*b*) the exposure rate was slightly higher in blacks than whites (8 *versus* 5%). The total age-adjusted incidence rate for pancreatic cancer for the three study areas combined during the study period was 16.0/100,000 in black men and 12.8/100,000 in white men, yielding a 25% excess in blacks. The complement of the PAR, the proportion of the disease not explained by heavy alcohol drinking, was applied to the total incidence rate to estimate the incidence in men who were not heavy drinkers (nondrinkers and men who drank fewer than 57 drinks/week). In the absence of heavy alcohol drinking, pancreatic cancer incidence rates would have been 14.2/100,000 for black men and 12.5/100,000 for white men, yielding a 14% excess in blacks.

Among women, alcohol drinking appears to be associated with increased risk in blacks but not in whites. Consequently, the PAR for alcohol was only estimable for black women. Sixteen % of pancreatic cancer in black women may be due to moderate-to-heavy alcohol consumption. The OR was higher in blacks than whites (2.0 *versus*

Table 4 *Numbers of cases and controls and ORs for pancreatic cancer according to wine consumption by race and sex*

Wine consumption	White				Black			
	No. of cases	No. of controls	OR[a]	95% CI	No. of cases	No. of controls	OR[a]	95% CI
Men[b]								
Never drank wine	113	487	1.0		64	486	1.0	
Ever drank wine	53	254	0.9	0.6–1.4	16	113	1.2	0.6–2.3
No. of glasses/wk[c]								
Never drank wine	113	487	1.0		64	486	1.0	
1–<7	32	164	1.0	0.6–1.6	8	74	1.1	0.5–2.7
≥7	19	84	1.0	0.5–1.8	8	33	1.6	0.6–4.2
Women[d]								
Never drank wine	115	301	1.0		82	318	1.0	
Ever drank wine	26	122	0.9	0.5–1.5	12	28	1.2	0.5–2.8
No. of glasses/wk[c]								
Never drank wine	115	301	1.0		82	318	1.0	
1–<7	16	98	0.7	0.3–1.3	9	20	1.3	0.5–3.5
≥7	10	24	1.4	0.6–3.5	3	7	1.0	0.2–4.6

[a] ORs adjusted for age, area, cigarette smoking, gallbladder disease, diabetes, hard liquor consumption, and beer consumption.
[b] ORs also adjusted for income.
[c] Two cases and 13 controls with missing information on amount of wine consumed were excluded from estimation of risk by amount consumed.
[d] ORs also adjusted for obesity.

Table 5 *Estimated %PARs for alcohol drinking by race and sex*

Race/Sex	Controls (% exposed)[a]	OR[b] for alcohol drinking[a] (95% CI)	%PAR[b] for alcohol drinking[a] (95% CI)	Total pancreatic cancer incidence rate	Pancreatic cancer incidence rate in nonexposed[c]
White men	5	1.4 (0.6–3.2)	2% [(−4)–8]	12.8/100,000	12.5/100,000
Black men	8	2.2 (0.9–5.6)	11% [(−1)–24]	16.0/100,000	14.2/100.000
White women	15	0.5 (0.3–1.1)	NE[d]	9.0/100,000	9.0/100,000
Black women	16	2.0 (1.0–3.9)	16% (1–31)	13.3/100,000	11.2/100,000

[a] Alcohol drinking in men, drank ≥57 drinks of alcohol/week; alcohol drinking in women, drank ≥8 drinks of alcohol/week.
[b] All ORs and PARs were adjusted for age, geographic area, cigarette smoking, income (men), gallbladder disease, diabetes, and obesity (women).
[c] Includes only men who were nondrinkers and those who drank <57 drinks/week and only women who were nondrinkers and those who drank <8 drinks/week.
[d] Because alcohol drinking was not related to increased risk (OR < 1.0), the PAR was not estimated for white women.

0.9), whereas the exposure rates were almost identical in black and white women (16 *versus* 15%). The total incidence of pancreatic cancer was 48% higher in black women than white women (13.3/100,000 *versus* 9.0/100,000). In the absence of moderate-to-heavy alcohol consumption, pancreatic cancer incidence rates would have been 11.2/100,000 for black women and 9.0/100,000 for white women, yielding a 24% excess in blacks.

DISCUSSION

Our results suggest that alcohol drinking at the levels typically consumed by the general population in the United States is probably not a risk factor for pancreatic cancer. We observed no overall association between alcohol drinking and pancreatic cancer risk, except among black women who experienced a nonsignificant 50% increased risk and white women who experienced a marginally significant 40% reduction in risk. Trends in risk with increasing alcohol intake were significant only among blacks and consistent only among black women. Rather, our data suggest that heavy alcohol drinking may be a risk factor for pancreatic cancer. Among men, blacks and whites who drank at least 57 drinks/week had ORs of 2.2 (95% CI = 0.9–5.6) and 1.4 (95% CI = 0.6–3.2), respectively. Among women, blacks who drank 8 to <21 drinks/week had an OR of 1.8 (95% CI = 0.8–4.0), and those who drank at least 21 drinks/week had an OR of 2.5 (95% CI = 1.02–5.9). However, white women with the same levels of alcohol intake experienced no increased risk. The excess risk seen among heavy drinkers did not appear to be due to residual confounding by cigarette smoking. When alcohol effects were examined among lifelong nonsmokers, risk estimates for heavy drinkers were either similar or higher than those observed for the total study group.

The increased risk observed for heavy drinkers, but not for light or moderate drinkers, may be explained by several factors: (*a*) it may suggest a toxic effect of heavy alcohol drinking; (*b*) because heavy drinking appears to be associated with only a moderate increase in risk, it may be difficult to detect an effect of lower levels of alcohol drinking using conventional epidemiological techniques; and (*c*) if nonrespondents were more likely to be heavy drinkers than respondents, selection bias could have resulted in an effect only among heavy drinkers. It appears unlikely, however, that such selection bias occurred. We compared the proportion of heavy alcohol drinkers in our control group to that observed in the HIS conducted in 1987.[4] The proportion of heavy drinkers among both blacks and whites was higher among our population controls than that observed in the HIS, suggesting that heavy drinkers were not underrepresented in our control group. For men, 4.9% of whites and 7.8% of blacks drank at least 57 drinks/week compared to 0.6% of whites and 1.3% of blacks in the HIS. For women, 2.6% of whites and 5.7% of blacks drank at least 21 drinks/week compared to 1.2% of whites and 2.1% of blacks in the HIS.

Our findings are consistent with those of most previous studies that have found little or no support for a causal relation between regular alcohol drinking and pancreatic cancer risk (18, 33). It is plausible, however, that heavy alcohol drinking could be a risk factor for pancreatic cancer. Chronic alcohol abuse is a known risk factor for chronic (calcifying) pancreatitis (34), which has been associated with increased pancreatic cancer risk in some reports (1, 35, 36). At least eight studies have suggested heavy drinkers may have an elevated risk (4–6, 8, 11, 13, 14, 17), although an effect among heavy drinkers has not been seen in other studies (37–43). Several possible explanations for the absence of risk among heavy drinkers observed in some studies are apparent: (*a*) cohort studies of alcoholics may not have been large enough to detect a modest elevation in pancreatic cancer risk; (*b*) case-control studies based exclusively on histologically confirmed cases may preferentially select cases with lower exposure to alcohol. Alcoholics may be more likely to be nonhistologically confirmed than nonalcoholics resulting from less access to medical care or cancer-related symptoms that are misdiagnosed as alcohol related (35). Because we included all likely cases, regardless of histological confirmation, our study was less prone to this type of selection bias; and (*c*) because of the unfavorable prognosis of patients with pancreatic cancer, many case-control studies included a high proportion of interviews with next-of-kin respondents. Data suggest that next-of-kin respondents reliably report whether a subject drank alcoholic beverages. Information on amount consumed, however, appears to be somewhat less reliable, and little is known about the ability of next-of-kin respondents to reliably report very heavy alcohol use (32). Thus, information obtained from next of kin on heavy alcohol drinking may be more vulnerable to misclassification than that based on more moderate levels of alcohol consumption.

We observed racial differences in risk with regard to the type of alcohol consumed. Risk among blacks was mainly due to consumption of hard liquor, whereas risk among white men was due to consumption of beer. Similar race-specific patterns of risk have been observed recently for oral (44) and esophageal (45) cancers. Reasons for the observed racial differences in pancreatic cancer risk by type of alcoholic beverage consumed are unclear. Previous studies of pancreatic cancer in whites in Switzerland (9), the United Kingdom (11), and the United States (13, 16) have suggested that beer consumption may be associated with increased risk, whereas studies in Japan (46), Poland (15), and the United States (16) have suggested that hard liquor may be associated with increased risk. Beer contains more nitrosamines than other types of alcoholic beverages (18), and nitrosamines are known pancreatic carcinogens in rodents (47). Hard

[4] L. Kessler, unpublished data (Food and Drug Administration).

liquor may also contain nitrosamines and a variety of other potential carcinogens (18), such as pesticides and contaminants of grain. In our data, risk appeared unrelated to the type of hard liquor consumed.

The effects of alcohol consumption on pancreatic secretion are poorly understood. It appears that alcoholic beverages added to the meal inhibit pancreatic enzyme secretion (48). Beer and hard liquor seem to have similar inhibitory effects on postprandial secretion of trypsin, whereas the effect of wine appears to be weaker (48). Inhibition of trypsin leads to secretion of cholecystokinin. Beer also has been shown to release significantly more cholecystokinin than do other forms of alcohol (48). Exogenous cholecystokinin promotes the growth of transplantable cell lines of human pancreatic adenocarcinoma (49).

Additional research focusing on the role of heavy alcohol drinking in pancreatic cancer etiology is needed. If heavy alcohol drinking is confirmed as a risk factor for pancreatic cancer in future studies, it may explain part of the excess risk experienced by blacks. In fact, we found that about one-third of the excess in black men and one-half of the excess in black women may be attributable to heavy alcohol drinking. The higher attributable risks for heavy alcohol drinking in blacks compared to whites (men, 11% in blacks and 2% in whites; women, 16% in blacks and 0% in whites) were primarily due to higher ORs associated with heavy alcohol intake in blacks; black and white population controls of each sex had somewhat similar prevalences of heavy alcohol consumption.

Several possible explanations for the higher alcohol-related ORs in blacks compared to whites are apparent. Blacks and whites may differ in their alcohol drinking habits. For example, blacks may drink different brands of beer and hard liquor than whites. We were unable to evaluate race-specific risks by brand name because information on brand consumed was not obtained. Blacks also may be more susceptible to alcohol-induced pancreatic cancer than whites because of race-related differences (genetic or induced) in either alcohol metabolism or vulnerability to pancreatic tissue damage from heavy alcohol use. Future research efforts should be directed at determining both the role of heavy drinking as a risk factor for pancreatic cancer and whether the risk of alcohol-related pancreatic cancer is greater in blacks than in whites.

ACKNOWLEDGMENTS

The authors thank Ruth Thomson (Westat, Inc.) for her assistance in study management and coordination; Roy Van Dusen and Douglas Flynn (Information Management Systems) for computer support; Holly Brown and Natalie Connor for clerical assistance; study coordinators, interviewers, and support staff in each study area for their diligent work; and the many physicians, hospitals, and study participants who cooperated in this study.

REFERENCES

1. Mack, T. Cancer by tissue of origin: pancreas. *In:* D. Schottenfeld and J. F. Fraumeni, Jr. (eds.), Cancer Epidemiology and Prevention, pp. 638–667. Philadelphia: W. B. Saunders Company, 1982.
2. Miller, B. A., Silverman, D. T., and Kaplan R. Pancreas. *In:* B. A. Miller, L. A. Ries, B. F. Hankey, C. L. Kosary, A. Harras, S. S. Devesa, and B. K. Edwards (eds.), Cancer Statistics Review 1973-1990. NIH Publication No. 93-2789. Bethesda, MD: National Cancer Institute, 1993.
3. Ishii, K., Nakamura, K., Ozaki, H., Yamada, N., and Takeuchi, T. Key questions in the epidemiology of cancer of the pancreas. Jpn. J. Clin. Med., *26:* 1839–1842, 1968.
4. Hakulinen, T., Lehtimaki, L., Lehtonen, M., and Teppo, L. Cancer morbidity among two male cohorts with increased alcohol consumption in Finland. J. Natl. Cancer Inst., *52:* 1711–1714, 1974.
5. Adelstein, A., and White, G. Alcoholism and mortality. Popul. Trends, *6:* 7–13, 1976.
6. Klatsky, A. L., Friedman, G. D., and Siegelaub, A. B. Alcohol and mortality: a ten-year Kaiser-Permanente experience. Ann. Intern. Med., *95:* 139–145, 1981.
7. Durbec, J. P., Chevillotte, G., Bidart, J. M., Berthezene, P., and Sarles, H. Diet, alcohol, tobacco and risk of cancer of the pancreas: a case-control study. Br. J. Cancer, *47:* 463–470, 1983.
8. Heuch, I., Kvale, G., Jacobsen, B. K., and Bjelke, E. Use of alcohol, tobacco and coffee and risk of pancreatic cancer. Br. J. Cancer, *48:* 637–643, 1983.
9. Raymond, L., Infante, F., Tuyns, A. J., Voirel, M., and Lowenfels, A. B. Alimentation et cancer du pancreas. Gastroenterol. Clin. Biol., *11:* 488–492, 1987.
10. Liang, J. D., Gao, Y. T., Zheng, W., and Wang, I. X. A case-control study of pancreatic cancer in Shanghai urban area. Tumor (Shanghai), *8:* 59–62, 1988.
11. Cuzick, J., and Babiker, A. G. Pancreatic cancer, alcohol, diabetes mellitus and gallbladder disease. Int. J. Cancer, *43:* 415–421, 1989.
12. Ferraroni, M., Negri, E., La Vecchia, S., D'Avanzo, B., and Franceschi, S. Socioeconomic indicators, tobacco and alcohol in the aetiology of digestive tract neoplasms. Int. J. Epidemiol., *18:* 556–562, 1989.
13. Olsen, G. W., Mandel, J. S., Gibson, R. W., Wattenberg, L. W., and Schuman, L. M. A case-control study of pancreatic cancer and cigarettes, alcohol, coffee and diet. Am. J. Public Health, *79:* 1016–1019, 1989.
14. Adami, H. O., McLaughlin, J. K., Hsing, A. W., Wolk, A., Ekbom, A., Holmberg, L., and Persson, I. Alcoholism and cancer risk: a population-based cohort study. Cancer Causes & Control, *3:* 419–425, 1992.
15. Zatonski, W. A., Boyle, P., Przewozniak, K., Maisonneuve, P., Drosik, K., and Walker, A. M. Cigarette smoking, alcohol, tea and coffee consumption and pancreas cancer risk: a case-control study from Opole, Poland. Int. J. Cancer, 601-607, 1993.
16. Zheng, W., McLaughlin, J. K., Gridley, G., Bjelke, E., Schuman, L. M., Silverman, D. T., Wacholder, S., Co-Chien, H. T., Blot, W. J., and Fraumeni, J. F., Jr. A cohort study of smoking, alcohol consumption, and dietary factors for pancreatic cancer (United States). Cancer Causes & Control, *4:* 477–482, 1993.
17. Tonnesen, H., Moller, H., Anderson, J. R., Jensen, E., and Juel, K. Cancer morbidity in alcohol abusers. Br. J. Cancer, *69:* 327–332, 1994.
18. IARC. Alcohol Drinking. IARC Monographs on the Evaluation of the Carcinogenic Risk to Humans. Vol. 44. Lyon, France: IARC, 1988.
19. Falk, R. T., Pickle, L. W., Fontham, E. T., Correa, P., and Fraumeni, J. F., Jr. Life-style risk factors for pancreatic cancer in Louisiana: a case-control study. Am. J. Epidemiol., *128:* 324–336, 1988.
20. Clavel, F., Benhamou, E., Auquier, A., Tarayre, M., and Flamant, R. Coffee, alcohol, smoking and cancer of the pancreas: a case-control study. Int. J. Cancer, *43:* 17–21, 1989.
21. Farrow, D. C., and Davis, S. Risk of pancreatic cancer in relation to medical history and the use of tobacco, alcohol and coffee. Int. J. Cancer, *45:* 816–820, 1990.
22. Ghadirian, P., Simard, A., and Baillargeion, J. Tobacco, alcohol, and coffee and cancer of the pancreas. Cancer (Phila.), *67:* 2664–2670, 1991.
23. Jain, M., Howe, G. R., St. Louis, P., and Miller, A. B. Coffee and alcohol as determinants of pancreas cancer. A case-control study from Toronto. Int. J. Cancer, *47:* 384–389, 1991.
24. Bueno de Mesquita, H. B., Maisonneuve, P., Moerman, C. J., Runia, S. and Boyle, P. Lifetime consumption of alcoholic beverages, tea, and coffee and exocrine carcinoma of the pancreas: a population-based case-control study in the Netherlands. Int. J. Cancer, *50:* 514–522, 1992.
25. Friedman, G. D., and Van Den Eeden, S. K. Risk factors for pancreatic cancer: an exploratory study. Int. J. Epidemiol., *22:* 30–37, 1993.
26. Waksberg, J. Sampling methods for random digit dialing. J. Am. Stat. Assoc., *73:* 40–46, 1978.
27. Breslow, N. E., and Day, N. E. Statistical Methods in Cancer Research, Vol 1. IARC Scientific Pub. No. 32:5-338. Lyon, France: IARC, 1980.
28. Dixon, W. J. (ed.), BMDP Statistical Software Manual, Vol. 2, pp. 1013–1077. Berkeley, CA: University of California Press, 1990.
29. Micozzi, M. S., Albanes, D., Jones, D. Y., and Chumlea, W. C. Correlations of body mass indices with weight, stature, and body composition in men and women in NHANES I and II. Am. J. Clin. Nutr., *44:* 725–731, 1986.
30. Bruzzi, P., Green, S. B., Byar, D. P., Brinton, L. A., and Schairer, C. Estimating the population attributable risk for multiple risk factors using case-control data. Am. J. Epidemiol., *122:* 904–914, 1985.
31. Benichou, J., and Gail, M. H. Variance calculations and confidence intervals for estimates of the attributable risk based on logistic models. Biometrics, *46:* 991-1003, 1990.
32. Graham, P., and Jackson, R. Primary *versus* proxy respondents: comparability of questionnaire data on alcohol consumption. Am. J. Epidemiol., *138:* 443–452, 1993.
33. Silverman, D. T., Dunn, J. A., Hoover, R. N., Schiffman, M., Lillemoe, K. D., Schoenberg, J. B., Brown, L. M., Greenberg, R. S., Hayes, R. B., Swanson, G. M., Wacholder, S., Schwartz, A. G., Liff, J. M., and Pottern, L. M. Cigarette smoking and pancreas cancer: a case-control study based on direct interviews. J. Natl. Cancer Inst., *86:* 1510–1516, 1994.
34. Woutersen, R. A., and Visser, C. J. Alcohol and cancer of the pancreas. *In:* R. Yirmiya and A. Taylor (eds.), Alcohol, Immunity, and Cancer, pp. 227–255. Boca Raton, FL: CRC Press, 1993.
35. Velema, J. P., Walker, A. M., and Gold, E. B. Alcohol and pancreatic cancer: insufficient epidemiologic evidence for a causal relationship. Epidemiol. Rev., *8:* 28–41. 1986.
36. Lowenfels, A. B., Maisonneuve, P., Cavallini, G., Ammann, R. W., Lankisch, P. G., Andersen, J. R., Dimagno, E. P., Andren-Sandberg, A., Domellof, L., and the International Pancreatitis Study Group. Pancreatitis and the risk of pancreatic cancer. N. Engl. J. Med., *328:* 1433–1437, 1993.
37. Sundby, P. Alcoholism and Mortality. Olso: Universitetsforlaget, 1967.
38. Schmidt, W., and de Lint, J. Causes of death of alcoholics. J. Stud. Alcohol, *33:* 171-185, 1972.
39. Monson, R. R., and Lyon, J. L. Proportional mortality among alcoholics. Cancer (Phila.), *36:* 1077–1079, 1975.
40. Dean, G., MacLennan, R., McLoughlin, H., and Shelley, E. Causes of death of blue-collar workers at a Dublin Brewery, 1954–73. Br. J. Cancer, *40:* 581–589, 1979.

41. Robinette, C. D., Hrubec, Z., and Fraumeni, J. F., Jr. Chronic alcoholism and subsequent mortality in World War II veterans. Am. J. Epidemiol., *109:* 687–700, 1979.
42. Jensen, O. M. Cancer Morbidity and Causes of Death among Danish Brewery Workers. Lyon, France: IARC, 1980.
43. Schmidt, W., and Popham, R. E. The role of drinking and smoking in mortality from cancer and other causes in male alcoholics. Cancer (Phila.), *47:* 1031-1041, 1981.
44. Day, G. L., Blot, W. J., Austin, D. F., Bernstein, L., Greenberg, R. S., Preston-Martin, S., Schoenberg, J. B., Winn, D. M., McLaughlin, J. K., and Fraumeni, J. F., Jr. Racial differences in risk of oral and pharyngeal cancer: alcohol, tobacco, and other determinants. J. Natl. Cancer Inst., *85:* 465–473, 1993.
45. Brown, L. M., Hoover, R. N., Greenberg, R. S., Schoenberg, J. B., Schwartz, A. G., Swanson, G. M., Liff, L. M., Silverman, D. T., Hayes, R. B., and Pottern, L. M. Are racial differences in squamous cell carcinoma of the esophagus explained by alcohol and tobacco use? J. Natl. Cancer Inst., *86:* 1340–1345, 1994.
46. Hirayama, T. Epidemiology of pancreatic cancer in Japan. Jpn. J. Clin. Oncol., *19:* 208–215, 1989.
47. Rao, M. S. Animal models of exocrine pancreatic carcinogenesis. Cancer Metastasis Rev., *6:* 665–676, 1987.
48. Hajnal, F., Flores, C. M., Radley, S., and Valenzuela, J. E. Effect of alcohol and alcoholic beverages on meal-stimulated pancreatic secretion in humans. Gastroenterology, *98:* 191-196, 1990.
49. Smith, J. P., Solomon, T. E., Bagheri, S., and Kramer, S. Cholecystokinin stimulates growth of human pancreatic adenocarcinoma SW-1990. Dig. Dis. Sci., *35:* 1377–1384, 1990.